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on February 5, 1997

TOWNSEND and TOWNSEND and CREW LLP

By Wanda Darren

PATENT

Attorney Docket No. 015270-002110

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
PETER A. SEUBERT et al.	Examiner: Patricia Duffy
Application No.: 08/419,008	Art Unit: 1818
Filed: April 7, 1995	DECLARATION PURSUANT TO 37 C.F.R. § 1.131
For: METHODS FOR AIDING IN THE DIAGNOSIS OF ALZHEIMER'S DISEASE BY MEASURING AMYLOID-β PEPTIDE (x-≥41) AND TAU	

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

We, PETER A. SEUBERT, CARMEN VIGO-PELFREY, DALE B. SHENK and ROBIN BARBOUR declare:

1. We are the named co-inventors of the inventions claimed in the above-captioned application. We make this declaration to present facts establishing that methods of measuring soluble Aβ(x-≥41) described in the above-captioned application were invented before January 1994. All the work described hereinbelow was performed in the United States of America.

2. Attached hereto at Exhibit 1 are copies of laboratory notebook pages numbered 52-55 and 58 kept by Carmen Vigo-Pelfrey. Carmen Vigo-Pelfrey signed these pages on the bottom left-hand side using her maiden name, "C. Vigo." The dates on these notebook pages indicated by Carmen Vigo-Pelfrey

is actually $A\beta_{33-42}$ with cysteine amino-heptanoic acid added at the amino terminus for purposes of conjugation to a carrier peptide.

5. In the sandwich assay described in the preceding paragraph, Carmen Vigo-Pelfrey stated that the second antibody was "277-2." Antibody 277-2 is specific for $A\beta_{1-42}$. (See also the specification, page 27, section b.)

6. Carmen Vigo-Pelfrey did not identify the capture antibody, stating only that "Plates were coated with 5 μg/ml and fixed with 0.25% HSA." However, the capture antibody is identified on page 58 of the notebook. That page refers to the detection of $A\beta_{1-42}$. There, in the middle of the page, Carmen Vigo-Pelfrey stated, "The assay was performed as described in p 52." Above that statement, the Plate Map section indicates the antibodies used: "266-272-2". "266" is a reference to the capture antibody. Antibody 266 is specific for the junction region of Aβ. (See also the specification on pages 25-27.)

7. The reference to "272-2" is, in our opinion, an erroneous reference to antibody "277-2". We are familiar with all of the antibodies used in these experiments conducted at Athena Neurosciences. We did not have any antibodies called "272-2".

8. Carmen Vigo-Pelfrey showed that the sandwich assay described could detect $A\beta_{1-42}$ and distinguish it from $A\beta_{1-28}$, $A\beta_{1-38}$ and $A\beta_{1-40}$. Pages 53-55 of the notebook show data produced using the above assay to generate standard curves for $A\beta_{1-42}$, $A\beta_{1-28}$, $A\beta_{1-38}$ and $A\beta_{1-40}$. The standard curve on page 55 shows the specific detection of $A\beta_{1-42}$ in the assay. Below the standard curve on page 55 Carmen Vigo-Pelfrey stated, "This assay detects $A\beta_{1-42}$ immunoreactivity with sensitivity greater than 0.625 and with no cross reactivity with $A\beta_{1-40}$, $_{1-38}$ or $A\beta_{1-28}$."

9. Thus, the notebook pages show the actual detection of $A\beta_{1-42}$ in a sandwich ELISA in which antibody 266, directed to

the junction region of Aβ, was used as the capture binding substance and antibody 277-2, directed to the carboxy terminus of $A\beta_{1-42}$, was used as the detection binding substance. In these experiments, the amount of binding by the detection binding substance was determined using a reporter antibody, which was an enzymatically labeled antibody specific for rabbit antibodies.

10. We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and, further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application of any patent issued thereon.

Date: January 28, 1997 — Peter A. Seubert

Date: January 24, 1997 — Carmen Vigo-Relfrey

Date: January 24, 1997 — Dale B. ~~Shenk~~ Schenk

Date: January 30, 1997 — Robin Barbour

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